Claim 12 has been added, support for which can be found, inter alia, the specification of the application as originally filed. No new matter has been added thereby.

Preliminarily, the Examiner objected to claims 8-11, appearing on pages 21 and 22 because text was missing due to photocopying. Accordingly, applicants submit herewith a clean copy of pages 21 and 22 (attachment A).

A change of correspondence address is being filed concurrently herewith to change the cover address to:

CHIRON CORPORATION
Intellectual Property Department
4560 HORTON STREET
EMERYVILLE, CA 94608-2916

An IDS was submitted on September 21, 2000. Applicants have not received initialed copies of the PTO 1449 forms submitted with the IDS. Accordingly, applicants request that the Examiner provide these copies in the next action.

The Examiner noted that, on page 13 of the specification, the headings for each column in Table 1 appear to be out of alignment. Applicants have amended Table 1 herein to correct the misalignment. This amendment is clearly to correct a typographical error. No new matter has been added by this amendment.

The Office Action asserts that the use of trademarks such as "FICOLL-HYPAQUE," at page 7, line 8, and "DYNABEADS" at page 8, line 8, should be capitalized whenever they appear in the specification in accordance with *MPEP 608.1 (V)* and *Appendix 1*. Applicant has amended the specification to comply with this requirement.

The Examiner noted that the above-identified patent application does not contain an abstract of the disclosure as required by 37 C.F.R. § 1.72(b). The specification has been amended herein to include a separate Abstract of the Disclosure ("Abstract"), which is also submitted herewith on a separate sheet of paper (Attachment B). Support for the Abstract can be found in, *inter alia*, the Examples and claims of the application as originally filed. No new matter has been added thereby.

Claim Objections

The Examiner requested that Applicant submit clean copies of claims 8-11 due to text missing because of photocopying. In accordance with the Examiner's request, applicant has submitted herewith a copy of claims 8-11 as originally filed. No new matter has been added thereby.

The Office Action objects to claims 3-11 under 37 C.F.R. 1.75(c) as being in improper form because multiple dependent claims are depending from other multiple dependent claims. Applicant has amended the claims to comply with this requirement.

Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-11 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 2, 7, 8, and 9 have been canceled. Applicant respectfully traverses these rejections as they apply to the remaining claims.

It is well settled that, when determining whether a claim satisfies the requirements of 35 U.S.C. § 112, second paragraph, the proper inquiry is "whether those skilled in the art would understand what is claimed when the claim is read **in light of the specification**." *See Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986) (emphasis added).

Applicant respectfully submits that those skilled in the art can understand what is claimed when the claims are read in light of the specification.

The Examiner asserted that the scope of claim 1 is unclear. Claim 1 has been amended herein to, *inter alia*, recite "*in vivo.*" Page 3, lines 31-35, of the application as filed, provides that the T cells may be activated *in vivo*, leading to an enhanced immunological response which may be used in a method of therapy comprising activating in a human or animal subject T cells using the method according to the invention.

The Examiner also asserts that it is unclear whether the method is intended to be limited to activation of purified populations of T cells, or if it encompasses activation of mixtures of cells (e.g. white blood cells) including T cells. The Examiner's concern appears to be predicated on the foregoing assertion that claim 1 is unclear as to its scope, *i.e.* whether it is intended to encompass both *in vivo* and *in vitro* activation of T cells. This rejection is obviated by Applicant's amendment of claim 1.

The Examiner also asserts that it is unclear whether antigen-independent activated T cells must eventually come into contact with processed antigen, or if the activated T cells are useful even if they do not specifically recognize antigens. On page 4, lines 3-14 it is disclosed that activated T cells produce desirable lymphokines useful in cell-mediated immune responses, such as interleukins, interferons and colony stimulating factors. It will also be possible to achieve isolated T cell activation and effector T cell recruitment in areas of specific immunological interest.

With respect to claims 5 and 6, the Examiner stated that it is unclear as to what the recited dosages therein refer. As previously stated, the proper inquiry into whether a claim satisfies the

requirement of 35 U.S.C. § 112, second paragraph, is "whether those skilled in the art would understand what is claimed when the claim is read **in light of the specification**." *See Orthokinetics Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986) (emphasis added). Applicant respectfully submits that those skilled in the art can understand what is claimed when the claims are read in light of the specification.

Rejections under 35 U.S.C. § 102(b) and (e)

Claims 1-6 and 9-12 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Chong, U.S. Patent No. 4,879,111. Claims 1-6 and 9-12 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Zimmerman et al., U.S. Patent No. 5,425,940. Only claims 1-11 were pending in this application. Claims 2 and 9 have been canceled. Applicant traverses these rejections as applied to the remaining claims.

It should be noted that inherency may not be established by probabilities or possibilities; nor is the mere fact that a certain thing may result from a given set of circumstances sufficient to establish inherency. *See Continental Can Co., U.S.A. v, Monsanto Co.*, 948 F.2d 1264, 1269, 20 U.S.P.Q. 2d 1746, 1749 (Fed. Cir. 1991). Unlike Chong and Zimmerman, et al., Applicant's claims do not require, *inter alia*, that TNF and IL-2 be administered in synergistically effective amounts. Applicant respectfully requests that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-6 and 9-12 were rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Chong, U.S. Patent No. 4,879,111 in view of Paul, Fundamental Immunology (1993). Additionally, Claims 1-6 and 9-12 were rejected under 35 U.S.C. § 103 (a) as allegedly being

unpatentable over Zimmerman et al., U.S. Patent No. 5,425,940 in view of Paul, Fundamental Immunology (1993). Only claims 1-11 were pending in this application. Claims 2 and 9 have been canceled. Applicant traverses these rejections as applied to the remaining claims.

The discussion of Chong and Zimmerman et al. is incorporated herein. Paul does not overcome the deficiencies of Chong and Zimmerman et al.

The Examiner alleged that although the claims do recite "antigen independent activation of T cells" the term "does not distinguish over the prior art methods as any effects of IL-2 or TNF-alpha on T cells would be intrinsic to the prior art methods because they teach exactly the same method step: contacting T cells with IL-2 and TNF-alpha." The Examiner is reminded, however, that that which is intrinsic is not necessarily known. Obviousness cannot be predicated upon what is unknown. *In re Rijckaert*, 28 U.S.P.Q.2d 1955, 1957 (Fed. Cir. 1993).

Neither Chong nor Zimmerman et al. teach the combination of IL-2 and TNF-alpha in the absence of antigen. Nor does Paul disclose or suggest using TNF or IL-2 on T cells not previously activated.

The Examiner's reliance on Paul as teaching that "IL-2 induces antigen-nonspecific lymphokine activated killer cells" is misplaced. Lymphokine activated killer (LAK) cells are natural killer cells which are distinguished from T cells in not requiring prior sensitization. (Stewart Sell, Immunology, Immunopathology and Immunity, 4th ed., Elsevier, N.Y., 1987, pp. 63-64) (copy attached). Moreover, in a more recent edition of Fundamental Immunology, Paul provides that "mature NK cells are not T cells." (Fundamental Immunology 4th Ed., Lippincott-Raven,

Philadelphia, 1999) (copy enclosed) Therefore, none of the references, either alone or in combination, teach or suggest the claimed invention.

Applicant respectfully requests that these rejections be withdrawn.

Obviousness-type Double Patenting Rejection

Claims 1-8 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-6 of U.S. Patent No. 6,074,635. The claims, as amended herein, recite a method for activating T cells *in vivo*, and thereby obviate this rejection.

Applicant reserves the right to respond to rejections over the prior art made of record, but not relied upon, at such time as they are raised.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicant requests an early notification of the same. If the Examiner feels a telephonic interview would be beneficial, the Examiner is requested to call the undersigned at (215) 564-8352.

Respectfully submitted,

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Dated: February 1, 2001

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